DETAILED ACTION

Election/Restrictions

Claims 23-44 are currently pending in the application.

Applicant's election of Group III (i.e. method for the treatment of peripheral neuropathies comprising administering an effective amount of cAMP modulator) in the reply filed on 10/29/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Thus, the requirement is deemed proper and is therefore made FINAL.

Claims 39-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group and species, there being no allowable generic or linking claim.

Priority

Acknowledgment is made of applicant's claim for foreign priority. It is noted, however, that applicant has not provided English translations of the French application as required by 35 U.S.C. 119(b). Thus, the priority date of the instant invention is July 15, 2003 (the date of the PCT application). Without the English translations, one cannot ascertain if the instant invention is present in the French application. Therefore, art prior to the PCT date, but not before the date of the French application may be cited against the claims.

IDS

The information disclosure statement filed 05/31/07 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it includes search report citations. Applicant is advised that a search report is not a published document and therefore is not properly listed § 609.05(a).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **(see M.P.E.P 608.01 (k))**.

Claims 33-34 are particularly vague and indefinite given that applicant is claiming ascorbic acid "derivatives" **(in sentence 2 of both claims)**, "preferable" ascorbic acid "derivatives" **(in sentences 5 of claim 33 and sentence 4 of claim 34)** and "particular" ascorbic acid "derivatives" **(in sentence 3 of claim 34)**. Given that applicant did not particularly point out what particular ascorbic acid "derivatives" may be encompassed in the invention or whether the preferred embodiment is a further limitation in the claims, one of ordinary skill in the art would not be able to fully ascertain the metes and bounds of the aforementioned claims.

As a result of the above inconsistencies, the aforementioned claims are unable to be examined as disclosed given that the scope of the claimed subject matter would not be able to be determined by one of ordinary skill in the art. However, for the purpose of examination, Examiner will construe that the stated species set forth in the claims are the sole intended ascorbic acid "derivatives".

Objection

Claims 31-34 are objected to because of the following informalities: improper format of a Markush claim (i.e. "selected from the group consisting of") (see M.P.E.P. 803.02). Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-28, 30-31, 35-36 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Geffard (U.S. 6,114,388, already cited by applicant and filed on an IDS 1449) in view of Pomerance et al. (J. Biol. Chem., 2000, pg. 40539-40546).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Geffard teaches a method of treating neurodegenerative diseases, infections, traumatic or toxic neuropathies, neurodegenerative diseases resulting from genetic diseases or proliferative diseases with polylysine conjugates (see abstract and column 11, preparation IV and claim 16). Geffard further teaches that this method of treatment further provides the use of polylysine conjugated with the antioxidant vitamin C (see column 3, lines 7-8 and column 5, lines 8-11). Furthermore, Geffard discloses that the conjugates of the invention may be particularly useful for diseases presenting neurodegenerative disorders such as Charcot-Marie-Tooth disease (i.e. hereditary neuropathies vs. instant claims 27-28), multiple sclerosis (i.e. demyelininating peripheral neuropathies vs. instant claim 24) and insulin-dependent diabetes (instant claim 30 and see column 5, lines 45-49).

Geffard does not teach a method of treating neuropathies using a cAMP inhibitor or a method for regulating cAMP expression.

Pomerance et al. teaches that forksolin (a positive activator of cAMP) can activate cAMP and lead to the subsequent activation of p38-MAPK (see Introduction, left column, page 40540, paragraphs 1-2 and figure 7C, page 40543). Pomerance et al. further teaches that ascorbic acid (i.e. vitamin C) pretreatment can inhibit cAMP-dependent activation of p38-MAPK suggesting an inhibitory role of vitamin C in cAMP regulatory pathway (see figure 7C vs. instant claims 23, 25-26 and 35-36).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Geffard with the knowledge of vitamin C as a cAMP inhibitor provided by Pomerance et al. since Pomerance et al. teaches that p38-MAPK can be activated by oxygen reactive species. Given that Geffard teaches a method of treating neuropathies using vitamin C and Pomerance et al. discloses that antioxidants such as vitamin C can regulate cAMP dependent pathways, one of ordinary skill would have been motivated to combine the method of Geffard with the disclosure of Pomerance with the expectation of providing a method that is efficient in treating pain and inflammation associated with peripheral neuropathy due to the presence of reactive species.

Claims 29 and 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geffard (U.S. 6,114,388, already cited by applicant and filed on an IDS 1449) as applicable to claims 23-28, 30-31, 35-36 in view of Djoneidi et al. (Gene, 2000, pg. 223-231).

The Geffard reference is as discussed above and incorporated by reference herein. However, Geffard does not address the treatment of type 1 Charcot-Marie-Tooth disease (CMT1) or the regulation of PMP22 protein.

Djoneidi et al. teaches that the major form of Charcot-Marie-Tooth disease is CMT1a that is characterized by deletion, duplication or point mutations of the PMP22 protein (see Introduction, page 223-224 vs. instant claim 29). Importantly, Djoneidi et al. further teaches that PMP22 protein expression is regulated by cAMP (see Discussion, page 230, paragraph 3 vs. instant claims 37-38).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Geffard in view of the knowledge of PMP22 protein provided by Djoneidi et al. since inhibition of cAMP would likely result in reduction and/or inhibition of PMP22 protein in Charcot-Marie-Tooth type 1 patients. Given that Geffard teaches a method of treating peripheral neuropathy such as Charcot-Marie-Tooth disease with a cAMP inhibitor, and Djoneidi et al. discloses that a subset of such disease (i.e. CMT1a) is characterized by overexpression and/or deletion of the

cAMP controlled protein PMP22, one of ordinary skill would have been motivated to utilize the method of Geffard with the disclosure of Djoneidi et al. with the expectation of a successful therapeutic treatment that is able to regulate (i.e. reduce or inhibit) the expression of PMP22 protein.

Claims 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geffard (U.S. 6,114,388, already cited by applicant and filed on an IDS 1449) as applicable to claims 23-28, 30-31, 35-36 in view of Austria et al. (J. of Pharm. Biom. Anal. 1997,Vol. 15, pgs. 795-801).

The Geffard reference is as discussed above and incorporated by reference herein. However, Geffard does not address the treatment of peripheral neuropathy using a cAMP modulator that is a vitamin C salt or ester or metal salts of phosphorylated ascorbic acid.

Austria et al. teaches that ascorbic acid species are well known in the art for their antioxidant properties. Austria et al. further teaches that vitamin C derivatives such as magnesium ascorbyl phosphate and ascorbyl palmitate (instant claims 32-34) were found to be more stable than vitamin C in solution (see abstract and figures 3-4, pg. 79).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Geffard with the ascorbic acid derivatives

disclosed by Austria et al. since these derivatives are more suitable and would be more suitable for pharmaceutical uses. Given that Geffard teaches a method of treating peripheral neuropathies with ascorbic acid and Austria et al. teaches ascorbic acid derivatives are more stable in solution than ascorbic acid itself, one of ordinary skill would have been motivated to combine the method of Geffard with the derivatives of Austria et al. with the expectation of providing a method of treatment that is therapeutically effective due to the usage of stable pharmaceutical compositions.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-5 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SJL

11/20/2007

/Cecilia Tsang/

Supervisory Patent Examiner, Art Unit 4137